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(54) Title: METHODS FOR THE IDENTIFICATION OF AGENTS THAT MODULATE THE STRUCTURE AND PROCESSING OF A MEMBRANE BOUND PRECURSOR PROTEIN

The amyloid cascade leading to Alzheimer's disease

Increased Aß production

Alzheimer's disease

Protofibril formation Aggregation of protofibrils into fibrils Plaque formation Inflammatory response Neuronal death

(57) Abstract: The present invention provides methods for the screening and identification of agents from a large library of molecular structures that can alter the cleavage of a membrane protein of interest. Agents identified by the methods of the present invention that modify the cleavage of the membrane protein can be used in the treatment and prevention of diseases such as inflammation, diabetes, cancer, Alzheimer's disease, Parkinson's disease, and the like. The methods select for and identify effector agents that bind to the membrane protein of interest causing a structural change in the structure of the membrane protein in such a way that the efficiency of the cleavage of a secretase is modulated. Further, the methods are carried out in an in vivo system that provides for physiological conditions similar or identical to conditions for membrane protein processing. Agents can be selected for their ability to cause a decrease or increase the amount of secretase cleavage of the membrane protein.

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